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CASES OF GENERALIZED FATAL BLASTOMYCOSIS, INCLUDING ONE IN A DOG *

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A number of cases of generalized fatal blastomycosis have been reported previously by Hektoen, Ricketts, Bassoe, Gilchrist, Hyde, Montgomery, Curtis, and others. We wish to add to the list of cases already published two more of the same kind occurring in man, while Dr. Maximilian Herzog furnishes a brief statement of a case of generalized fatal blastomycosis in a dog, apparently the only one in this species of domestic animal ever observed. Blastomycosis in the horse has been observed in various countries a number of times, tho it is now claimed that most of what heretofore has been described as equine blastomycosis is really a sporotrichosis.

The micro-organisms from the human cases reported in this paper, have been examined fully by cultural methods and also by animal experiments. The blastomyces obtained in pure cultures from two generalized fatal cases and from a cutaneous case, did not appear to be very virulently pathogenic for the animals used in the experiments, tho lasting pathologic lesions were produced in some animals, as will appear from the detailed report which follows.

CASE 1

The patient was an Italian street laborer, 30 years old, married, with 2 healthy children. His parents were living and in good health; his 4 brothers and 2 sisters were also all living and well. Patient denied syphilis or any severe previous illness. Usual weight 140 pounds. While working as an excavator for a gas main, October 4, 1913, he was troubled with a cough which was diagnosed as bronchitis. There was considerable expectoration, but no tubercle bacilli were found. The patient complained of dizziness. A warty growth of the upper lip was first noticed by the patient the latter part of December, but this was not accompanied by pain, soreness or itching; there were no other skin lesions at this time. Early in February, 8 abscesses began to form in various places over the body. The patient's temperature throughout ranged from 99 to 102 F., pulse from 90 to 100, respiration from 20 to 26, and there was up to February, 1914, a great loss of weight.

Treatment: The bronchitis was treated with the usual remedies, but with little improvement; as the abscesses developed, however, the cough practically disappeared. A number of the abscesses were lanced, and cleansed with tincture

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of iodin; one was entirely healed, and the others were improved. The growth on the lip received applications of copper sulfate, which reduced the size of it somewhat. Internally potassium iodid was administered in large doses, also with copper sulfate in 1/6-gr. doses. April 11, 1914, the patient's condition was much improved, and there was decided gain in weight. The patient was seen again in May, after which he was lost track of, until his death. Postmortem examination was not permitted.

CASE 2

The patient was a woman 60 years old, an Italian, married (family history not obtainable). The woman had worked in a cellar sorting winter cabbages for many years. She had been troubled with a painful cough for over a year. After an accident in which she had fallen backward downstairs into the cellar, her arm became swollen and remained that way for 3 months. The cough was persistent until death. The body was literally covered with blastomycotic ulcers. No other history was obtainable and postmortem examination was not permitted.

CASE 3

The patient, an American machinist, aged 20, came to the clinic with a lesion on the ventral surface of the left wrist; no other complaint. Gonorrhea and syphilis denied, family history negative. The patient claimed that the lesion started as a pimple, which was accompanied at the onset with itching; it soon broke and discharged a glairy tenacious pus. The lesion, which kept getting larger, at the time of the examination was 3 by 1½ inches, with a slightly raised margin, and a dark varicose surface, scattered throughout which were little sinuses. Upon examination it was found that the patient was very sensitive to pain; on removal of the scab, a thick yellow discharge could be pressed out. Older areas of the ulcer had healed with cicatrix formation. Tubes were inoculated after the discharge had been examined in KOH solution, and after round doubly contoured bodies had been found. The patient had been working in a basement in Chicago for the past 6 months. On entering the clinic, he was given potassium-iodid treatment in large doses with the result that by November, 1914, the lesions had healed, leaving a dark disfiguring scar.

CULTURES

In Case 1, Dr. Maximilian Herzog and Dr. Margaret S. Grant obtained the blastomycotic organism from a blood culture, prepared in the usual manner. About 10 c.c. of the blood were drawn under all possible aseptic precautions from a vein of the patient's arm, and added at once to sterile broth in a flask and to agar tubes, which were then incubated. The cultures which developed first appeared, after from 3 to 4 days, as small colonies, granular and moist, dirty-white in color, and firmly adherent to the solid culture media. In the other two cases reported in this paper, the organisms were obtained from the cutaneous lesions.

The cultural characteristics of the organisms from the three cases studied were so similar that one common description for all may be given, with certain differential features, however, as will be pointed out.

Agar Plates, Slants, and Stab Cultures.—Aerobic growth; no growth anaerobically. On the agars—ascitic, glycerin, glucose, maltose, beer wort + 10 oxalic glucose + 10 oxalic lactose, and nutrient agar—the growth appeared on the late 3rd and early 4th days as little moist colonies, granular and pinpoint in size, very firmly attached to the media and difficult to remove, the colonies later

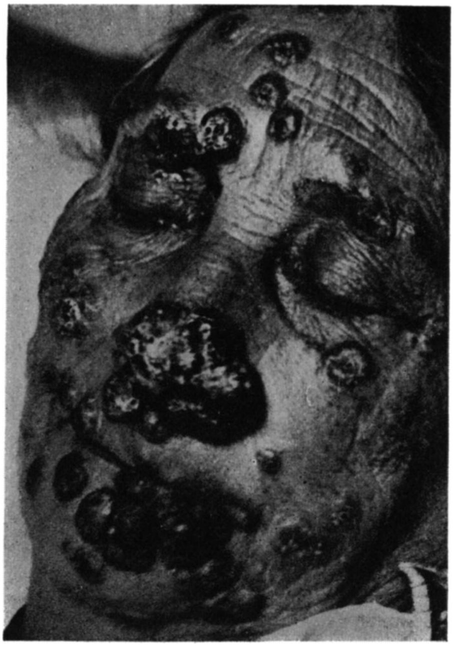


Fig. 1. Photograph of the face of Patient 2.

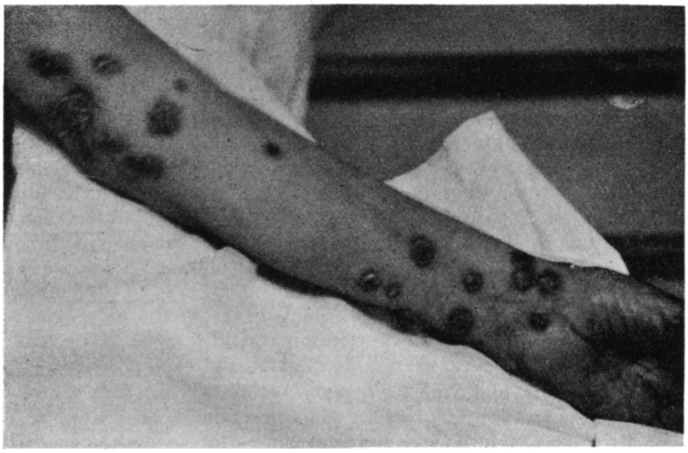


Fig. 2. Photograph of the arm of Patient 2, showing dermal lesions of blastomycosis.

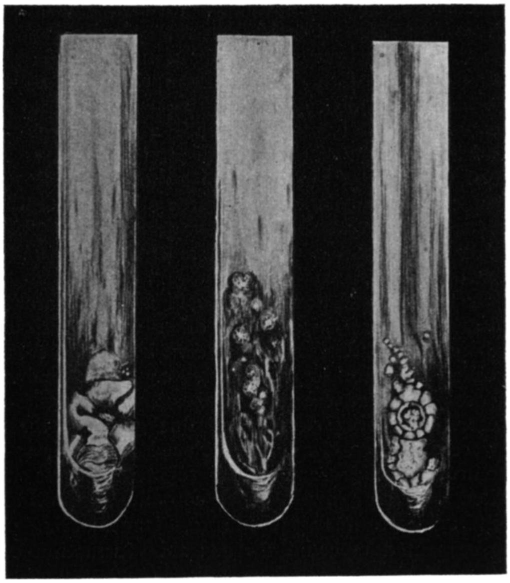
becoming umbonate in shape. In from 7 to 10 days fine delicate aerial hypae presented themselves. In from 12 to 15 days the colonies grew rapidly and presented a granular dirty-gray base supporting a fine raised white center from which, as mentioned in regard to colonies from Case 1, bush-like prominences (aerial hypae) sprang (Fig. 3b). The surface now became uneven with an outgrowth of fine delicate closely woven threads, visible to the naked eye, which, being branched and at the edge of the growth attenuated, gave a ciliated appearance to the edge of the colony. In order to remove the colonies it was necessary to break the culture media with a strong platinum loop. The downy growth spread until after from 29 to 30 days it almost filled the tubes or covered the surface of the plates (Fig. 4), and generally showed small white spherical bodies throughout.

On glucose agar the growth was more rapid and the colonies became more coarsely granular and varicose than on the other media; microscopic examination showed the delicate threads that grew down into the media to be composed of segmented mycelia and round or oval doubly contoured buds. The segmented mycelia on all agars presented the same appearance, being from 4 to 6 to 10 microns in diameter, containing coarse and fine granules throughout the protoplasm. There were also seen clear, pink-colored, generally spherical vacuoles; nucleus-like structures were present in the segments; buds were seen in the more densely packed mycelial growth, which contained from 2 to 4 to 5 spherical bodies packed within the granular protoplasm. One budding process was seen coming off each segmented mycelial thread; this formation extended, became segmented, and formed new mycelial growths.

On glycerin agar the colonies as on other agars appeared in from 3 to 5 days, but did not present the coarsely granular appearance so pronounced on agar or glucose agar. The colonies on the 12th and 15th days showed slight cracks occurring in the surface, soon presenting the picture of a crumpled cloth (Fig. 6), all other characteristics remaining the same.

On ascitic agar aerial hypae were less pronounced. Maltose-agar and beer-wort-agar growths showed the same characteristics as the growths on other agars. Nutrient agar growth was marked by fine granular moist pinpoint colonies that appeared on the 4th and 5th days. The growth was slower and poorer on this medium than on any of the other agars. Pieces of agar growth were used in 3 cases on Dogs 1 and 2 for inoculations.

Broth.—On + 10 acid, neutral, or — 10 alkaline broth growth occurred with no noticeable differences on the 4th and 5th days, but it was not so thick and luxuriant as on 2% glucose broth. Up to the 12th day of growth the colonies appeared as fine white fluffy balls, adherent to each other, and looking like thistle-down. No separation of these colonies occurred until after from 15 to 18 days' growth in all 3 cases. In cultures from Cases 2 and 3 after the 4th and 5th generation the colonies separated easily upon shaking. Top growth was not characteristic of any one of the three strains, but a bottom growth was typical; when, however, the growth had filled most of the liquid medium, i. e., in 5 or 6 weeks, a top growth also occurred. In cultures from Case 1, coarse spike-like aerial hyphae were present, springing from the top growth for 3 generations before the conditions ceased. The individual colonies were uniform in density, showing a dark-gray granular center, with fine closely woven offshoots which looked like projecting cilia at the edge of the floating colonies; 2 dark encircling rings showed in the older growths, due to the compact old growth of mycelial threads and the beginning of the younger straighter threads.



(a) (b) (c)

Fig. 3. (a) Pure culture, 6 months old, on glycerin agar, of the organism obtained from Patient 1. The culture was kept at room temperature. (b) Pure culture of the same organism after 7 days' growth on glucose agar in the incubator at 37 C. (c) Pure culture, 4 months old, on glycerin agar, kept at room temperature. Organism from Patient 2.

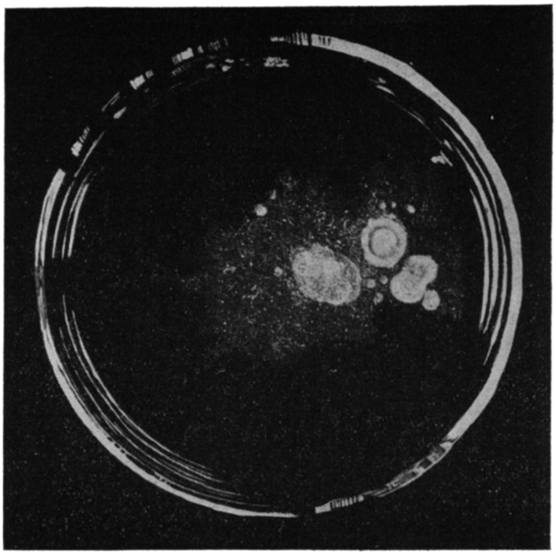


Fig. 4. Pure culture, 60 days old, on agar in a petri dish kept in the incubator at 37 C. Organism from Patient 2.

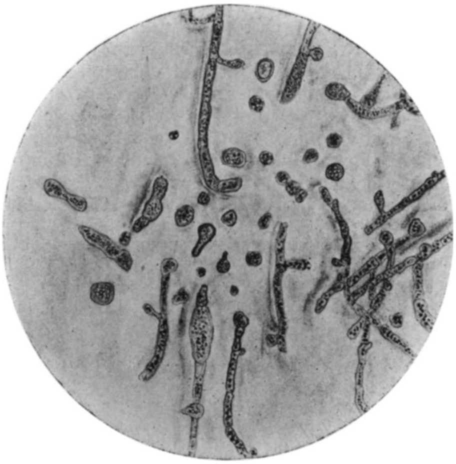


Fig. 5. Microscopic preparation of organism from Patient 2, from a young colony of a culture from 10 to 12 days old, showing formation of buds and mycelial threads. Spores in center of buds. Oil-immersion magnification.

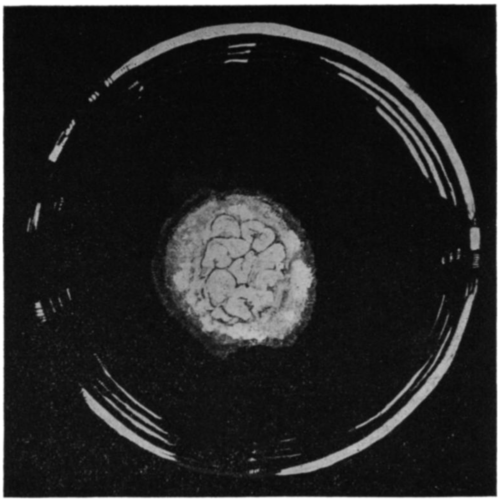


Fig. 6. Pure culture, 60 days old, on glycerin agar, kept at incubator temperature of 37 C. Organism from Patient 2.

Top growths soon became covered by a fine downy filamentous covering, dry and white in appearance. The growth was tenacious and resisted breaking up, but whole colonies could be completely removed with the platinum loop. Older colonies showed a degenerative change in the center, surrounded by gray granular spots (Fig. 7) ; growth consisted chiefly of mycelial threads with round or oval forms, scattered in the more tangled older threads. The microscopic findings were the same as on other media.

Broth cultures shaken with glass beads in physiologic salt solution were injected in 2- and 5-c.c. amounts, subcutaneously and intraperitoneally, into Guinea-pigs 1, 2, and 3, below, and behind the shoulder, and into Rabbits 1 and 2, and an atomizer was used to spray the animals with a view to producing the pulmonary form of blastomycosis if it could be produced. Rabbit 3 was injected intravenously. White Rats 1 and 2 received intravenous injections together with subcutaneous injections of 0.5 c.c. of bead-macerated broth. White Mice 1, 2, and 3, and Gray Rats 1 and 2 received the same.

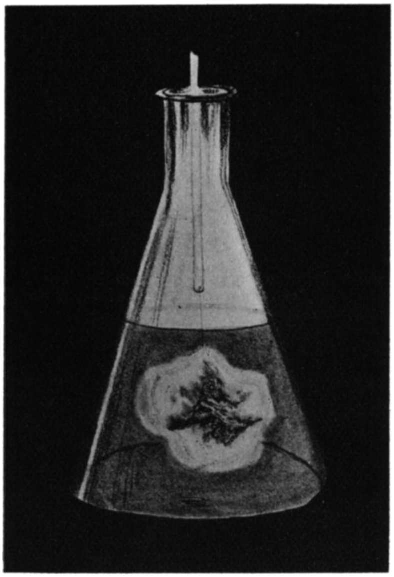


Fig. 7. Pure culture in nutrient broth, 40 days old, kept at room temperature. Organism from Patient 3.

Koch's Blood Serum and Oxblood Serum.—Growth occurred, as on other media, on the 3rd and 4th days as small gray pinpoint colonies, with fine ciliated edges growing out and into the media, the spike-like aerial hyphae being blunter and coarser, in cultures from Case 1, than on other media. All colonies grew rapidly and on the 10th day of growth the heavy wrinkled bases grew together, giving the surface a rugose or verrucose appearance. The colonies were so firmly incorporated into the media that removal necessitated a considerable amount of force, the growth coming away as a thick tenacious covering 1/32 inch in thickness. The fine downy mouldy growth was never as prominent on any blood medium as on the other media. Cultures from Case 3 liquefied both

Koch's and ox-blood media, those from Cases 1 and 2 did not; those from Cases 1 and 2 standing at cool temperature soon showed evidence of liquefaction.

Dorsett's Egg Medium.—Cultures from Case 1 grew better than those from Cases 2 and 3, but growths were neither rapid nor luxuriant as on other media.

Milk.—Growth showed as a bottom growth within 20 days, a falling down to the bottom of the tube of the solid constituents occurring, the supernatant fluid remaining as a clear upper stratum. No coagulation. In litmus milk the changes produced were the same as in ordinary milk; no change in color, no acid reaction after 20 days.

Conradi-Drigalski Medium.—No growth.

Potato and Carrot.—Growth occurred in from 3 to 4 days as dirty-white pinpoint moist colonies, doubling themselves in size in 3 days, while fine delicate mycelia were sent out over and into the media. Growth from the 7th day on was very rapid, and covered by a white fine downy mould-like formation; surface wrinkled quickly and was resistant to efforts at removal. On these media the growth strongly resembled that of an older growth in glycerin-agar tubes. Microscopic findings were the same as on other media.

Fermentation of Saccharose, Maltose, Dextrose, Levulose, Lactose and Mannite.—Cultures from Case 1 fermented all sugars with the production of CO_2 and alcohol for 2 generations. Inoculations into sugar media afterwards from agar growth after 5 months failed to ferment sugars; inoculations made 8 months afterwards from Koch's blood serum failed to ferment the media. Cultures from Cases 2 and 3 did not ferment any of the different sugar media tried.

Gelatin.—Growth occurred along the needle tract out and into the media as fine delicate rays. No liquefaction.

Potassium Iodid 5% Solution in Broth and Glucose Broth.—Growth was typical as on other liquid media, but the individual colonies were a trifle smaller.

ANIMAL EXPERIMENTS

Dogs 1 and 2, Cases 1, 2, and 3, were inoculated intraperitoneally with macerated agar growth, and pieces of growth on agar-agar were implanted subcutaneously. Reactive nodules appeared in from 4 to 6 days, finally enlarging to the size of a walnut; these nodules were tense and elastic, but did not fluctuate. The nodules diminished in size in from 2 to 4 weeks and then disappeared. Postmortem findings were negative.

Guinea-pigs 1, 2, and 3, Cases 1, 2, and 3, were inoculated with from 2 to 5 c.c. of bead-macerated broth cultures in physiologic salt solution subcutaneously and intraperitoneally. The animals also were exposed to a spray directed against the face.

Guinea-pig 1, Case 1, inoculated intraperitoneally, showed slight malaise in 5 hours and on the 2nd day a hot painful swelling occurred in the right testicle with great malaise. On the 11th day all evidences of scrotal trouble had disappeared. The guinea-pig resumed its normal habits and no other lesions were present. After 3 months the animal, on its back, showed a hard firm nodule, very itchy and situated just to the left of the median line. This nodule enlarged to the size of a hickory nut, becoming as it enlarged doughy and painful to the touch. The tumor-like mass covered the last dorsal and first 3 lumbar vertebrae. On the 5th day after appearing, the mass broke and discharged a glairy reddish-yellow pus, which upon examination in KOH solution showed round doubly contoured bodies. Inoculations were made into glucose-agar slants and the micro-organism obtained in pure culture. They grew by mycelial formation alone without any budding, and in 1 month had almost filled the tube. The abscess healed completely and at no time during the second attack, the first being represented by the scrotal swelling, was the animal in poor spirits.

Guinea-pigs 2 and 3, Case 1, and Guinea-pigs 1, 2, and 3, Cases 2 and 3, showed slight reactive nodules in from 4 to 5 days, which soon disappeared. Findings after the animals were killed, were negative, including blood cultures.

Rabbits 1 and 2, Cases 1, 2, and 3, received subcutaneous and intraperitoneal inoculations of 2 and 5 c.c. of broth culture which had been shaken with beads, and Rabbit 2, Cases 1, 2, and 3, received 0.5 c.c. injections into the marginal ear vein. All rabbits except Rabbit 2, Case 1, showed negative findings. Rabbit 2, Case 1, showed with other rabbits a small tense nodule at the site of inoculation and slight malaise. In 4 months a hard painful itchy tumor-like mass was felt over the costal cartilages of the ribs. On the right side and located directly under the skin in the cubcutaneous tissue, it seemed to be attached to the osseous structures underneath. This lesion was followed by a swelling of the left metatarsal region, which lasted only 10 days. A small hard palpable nodule was also found on the right ventral surface seemingly attached to the underlying muscles and fascia beneath. Appetite was still good; no nervousness or emaciation was present. At times the animal bit and scratched the areas described. The mass on the right side increased to the size of an apple. At the end of 5 months and 20 days Rabbit 2 was killed. The tumor-like mass had not ruptured and was still firm to the touch, with a fluctuating center. It was not attached to the underlying or overlying structures, but was situated in the subcutaneous areolar tissue and consisted macroscopically of a white fibrinous capsule, 1/8 inch in thickness, filled with a firm white cheesy mass, traversed by connective-tissue septa. The nodule on the abdominal fascia presented a similar picture. Spraying cultures into nostrils of all rabbits and guinea-pigs at intervals of from 2 to 5 days produced negative results.

Microscopic Findings.—The large tumor-like mass in the rabbit showed connective tissue septa enclosing a granular mass of large epithelioid cells and leukocytes with no micro-organisms present. Liver showed congestion with focal necrosis scattered throughout, but no micro-organisms. Kidneys were congested with beginning parenchymatous nephritis. Lungs showed small necrotic areas with the formation of giant cells; no micro-organisms present.

White Rats 1 and 2, Gray Rats 1 and 2, Cases 1, 2, and 3, each received intravenous and subcutaneous injections of 0.5 c.c.. Reactive nodules appeared at the sites of inoculation with slight malaise, recovery following in from 5 to 6 days. Upon 2nd inoculations the animals showed a dull listless attitude which lasted from 9 to 10 days. White mice 1, 2, and 3, Case 1, 2, and 3, received intravenous and subcutaneous injections with the same reactive results as in the case of the rats, only one mouse dying. Postmortem findings proved negative in all but Mouse 1, Case 1. In this mouse the lungs were studded with small gray nodules, which when fixed in formalin and embedded in paraffin showed small foci of necrosis with invasion of leukocytes, epithelioid cells, and giant cells with partly disintegrated yeast-like bodies. Kidneys highly congested, showing slight parenchymatous nephritis. Liver highly congested. Spleen normal and other organs apparently normal. No cultures were obtained by inoculation from internal organs or blood. Specimens stained with eosin methylene blue, hematoxylin and eosin, and gram's stain.

SUMMARY

Summarizing the observations and experiments that have been given thus in detail, we find that the clinical history of the cases agrees with that furnished by other investigators who have reported that living in basements or underground habitations predisposes to blastomycotic infection (Stober[1] and others). The primary lesions as found by Hektoen,[2] Montgomery,[3] LeCount and Bechtel,[4] and others, are identical with those described here and with those previously reported. Patients 1 and 2 complained of cough and severe pains in the chest, while Patient 3 gave the history of a pimple starting the cutaneous lesions. The only gross differences between the pure cultures were the spike-like prominences in those from Case 1 and their power to ferment sugar for 2 generations, while the organisms from Cases 2 and 3 possessed the power to liquefy blood serum. It is probable that the three organisms were identical, as most of the gross variations in the culture media observed in Case 1, appeared in the other two in time. This agrees also with the findings of Hamburger,[5] Montgomery and Ormsby,[6] and others. The aerial hyphae were more prominent in the spring and summer, while the rugose moist colonies were more common in the fall and winter. Growth by mycelial formation occurred most commonly, altho the incubator temperature favored a budding growth, but at no time in excess of mycelial formation. All growths were firmly incorporated into the solid media, so that it was necessary to break the culture media in order to remove the colonies.

Microscopic observations were made in the hanging drop in order to find out the method of reproduction, and it was in one instance possible to observe a growth with a projection of the protoplasm resembling a pseudopodium, which again in time formed a complete new mycelial segment. Granules and spherical ball-like particles as described by Ricketts[7] and others appeared in from 8 to 24 hours. After the formation of well-established lateral projections, nuclear-like bodies containing refractile and motile granules were observed, but no staining methods could demonstrate them later.

Beer-wort and nutrient-broth growths of all three strains were poured on gypsum blocks and kept at room temperature. The organisms were examined at the end of 12, 24, and 36 hours; after 24 hours the cultures from all cases showed round spherical endospores in the bud-like formation, numbering from 1 to 4 and 5 spore bodies. Tubes

[1] Arch. Int. Med., 1914, 13, p. 509.
[2] Jour. Am. Med. Assn., 1907, 99, p. 1071.
[3] Jour. Cutan. Dis., 1901, 19, p. 26.
[4] Arch. Int. Med., 1914, 13, p. 609.
[5] Jour. Infect. Dis., 1907, 4, p. 201.
[6] Arch. Int. Med., 1908-09, 2, p. 1.
[7] Jour. Med. Research, 1901, 6, p. 373.

of the organisms were sent to Mr. Richard Wahl[8] for examination as to spore-formation. The following report was received:

> Cases 1, 2, and 3 were inoculated in hopped wort with a specific gravity of 1.0488, unhopped wort of the same specific gravity, and boullion made the usual way and placed at 25 C. for 48 hours. At the end of this time, the hopped wort inoculated with Stems 1, 2, and 3, showed no signs of development. These samples were again examined after four days and showed no signs of development. The bouillon sample inoculated with Stems 1, 2, and 3 were examined after 48 hours and also after 4 days. They showed a development, but compared with the distillers' and brewers' yeast, the development was slow. The unhopped wort also developed slowly compared with brewers' and distillers' yeasts. This was the medium used for the endospore test. Three flasks of unhopped wort were inoculated with Stems 1, 2, and 3, and placed on gypsum blocks and placed at 25 C. An examination after 24 hours showed distinct endospores in all cases. Most of the cells contained one endospore, but some contained two and occasionally one contained three.

TABLE 1

DIFFERENTIAL FEATURES OF THE THREE STEMS OF ORGANISMS

Gross Cultural Appearances

Source of Cultures				Preferred Media					Solid Media										Liquid Media					Litmus Milk			Plates			
									Early		Later								Early		Later									
	Blood	Pus	Incubation period of cultures (Days)	Aerobic	Acid 1%	Alkaline 1%	Neutral	Saccharin	Elevated pinpoint	At first granular	Elevated	Wrinkled	Coherent and incorporated with media	White	Dirty gray	Brown with age	Growth into media		Bottom growth	Colonies adherent	Top growth	Colonies separate	Coagulation, milk	Acid	Alkaline	Neutral	Granular	Spreading by hyphae	Liquefaction blood	Liquefaction gelatin
Herzog-Grant I	+	*	3-4	+	+	+	+	++	+	+	+	+	+	+	+	+	+		+	+	+	±	—	—	—	+	+	+	+	—
Grant-MacLane II	*	+	3-4	+	+	+	+	++	+	+	+	+	+	+	+	+	+		+	+	+	±	—	—	—	+	+	+	+	—
MacLane...... III	*	+	3-4	+	+	+	+	++	+	+	+	+	+	+	+	+	+		+	+	+	±	—	—	—	+	+	+	+	—

+ = affirmative.
— = negative.
± = inconstant or moderate.
? = not satisfactory.

The behavior of the micro-organisms in saccharin and milk media would also indicate that they represent one species. Animal inoculations generally were not successful, tho others frequently have reported positive, fatal results. While inoculating rats intravenously, a point of a syringe came off, allowing a thick emulsion of micro-organisms to be precipitated into the eye of one of the assistants, and also a syringe point contaminated with blastomyces was introduced into the finger of an assistant accidentally, with no ill results in either case in one year from the time of the inoculations. A swelling of the testicle of a guinea-pig as reported by Hektoen also occurred in one of our animals, but at no time was it as extensive as the reaction with B. mallei. A pure culture of blastomyces killed by heating at 65 C. for 1 hour, was rubbed into the scarified arm of a woman suffering from sporotrichosis, but no inflammatory or other changes occurred on the arm so treated. The agglutination test with this patient's blood serum also proved negative when tried with an emulsion of blastomyces.

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[8] Biological Laboratories, Wahl Efficiency Institute for Baking Research, Chicago.

TABLE 1—*Continued*

DIFFERENTIAL FEATURES OF THE THREE STEMS OF ORGANISMS

Gross Cultural Appearances								Morphology																									
Fermentation						Products		Spherical		Mycelial				Capsule		Protoplasm						Reproduction						Aerial		Thermal Limits			
																						Tissue			Cultures, Surface and Submerged								
Saccharose	Maltose	Dextrose	Levulose	Lactose	Mannite	CO_2	C_2H_5OH	In tissue	In culture	In tissue	In culture	Mycelial diameter in microns	Spherical diameter in microns	In tissue	In culture	Finely granular	Coarsely granular	Vacuoles	Small movable granules	Nucleus	Endospores	Budding	Hyphae with segmentation	Endospores	Budding	Hyphae with segmentation	Lateral or terminal conidia	Lateral conidia	Ascospores	Killed by freezing	Killed by drying	Death point	Pathogenicity to animals
± +2	± +2	± +2	± +2	± +2	± +2	± +2	± +2	+	+	—	+	4-6-8	10-30	+	+	+	+	+	+	?	+	+	—	*	+	+4	+	+	*	*	*	*	+
—	—	—	—	—	—	—	—	+	+	—	+	4-6-8	10-20	+	+	+	+	+	+	?	+	+	—	*	+	+	+	+	*	*	*	*	—
—	—	—	—	—	—	—	—	+	+	—	+	4-6-8	10-20	+	+	+	+	+	+	?	+	+	—	*	+	+	+	+	*	*	*	*	—

+2 = to second generation.
* = no information in our finding.
+4 = forms large aerial Hyphae becoming smaller, disappears 4th generation.

The exact botanical classification of the organisms usually called blastomyces in medical literature is still doubtful. Whitman[9] in a contribution to the botany of the organism of blastomycosis, calls attention to this fact and asserts that he has been able to observe in a case of fatal systemic blastomycosis, sporangium formation of the ascus, enabling him to properly classify the organism. The name blastomyces was first used by Gilchrist and Stokes, who were first to report an American case, and who had noticed the yeastlike character of the micro-organism and its tendency to multiply extensively by budding. Ricketts thought that the so called blastomyces properly belonged to the family Oidium, while Ophüls suggested the designation coccidioides or coccidioidal oidiumyces. Whitman in sections of the tissues from his case found groups of spherical bodies contained in a capsule consisting of a dense nonstaining membrane about 10 microns thick. The capsules were round or slightly oval and within them were found a large number (up to 50 or more) of round or slightly reniform bodies approximately 7 microns in diameter, lying closely packed together in the sac. He also claimed that places were seen where the ascus had ruptured and had discharged its spores into the neighboring tissues, where they had become enlarged with unequal rapidity, so that one could see spores of every size from the smallest to the largest. From these observations Whitman came to the conclusion that the organism of blastomycosis is an ascus-producing fungus, and he placed it according to the classification proposed by DeBeurman and Gougerot among the exoasaceae as a new genus, Zymonema, which are vegetable organisms of mixed characters, that is, yeast forms and mycelial threads. However, Whitman is compelled to confess that he has never been able to get any ascus-formation in his pure cultures, and he says:

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[9] Jour. Infect. Dis., 1913, 13, p. 85.

> Cultures from the case have been grown on various media and have been observed for about one year, without disclosing more than what other observers have recorded. One finds the mycelial threads septate and branching, at irregular intervals chlamydospores, conidiospores forming either at the end of the hyphae or in continuity, the conidiospores in chains and separated by septa, in which case they represent the oidium type of spore-formation. The conidiospores are at first elongated, later they become more and more spherical and are finally set free, to become apparently the yeast-cell bodies from which the organism earned its earliest name. It is worth noting that the conidia-bearing hyphae are larger and denser than the vegetative threads.

A CASE OF GENERAL BLASTOMYCOSIS IN A DOG

Dr. Maximilian Herzog furnishes the following statements concerning an incomplete observation on a case of undoubted general blastomycosis in a dog: A few years ago he received at the laboratory of pathology of the Chicago Veterinary College, a specimen of the lungs of a dog. It was said that this dog had been suffering from a wasting disease and had finally died from it and that the most marked changes

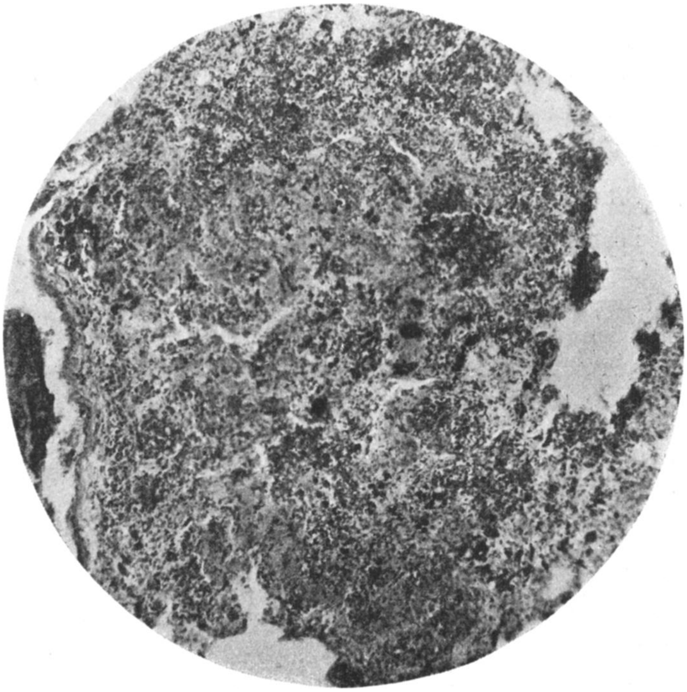

Fig. 8. Blastomycotic nodule in the lung of a dog, dead from generalized blastomycosis. Photomicrograph. Low magnification.

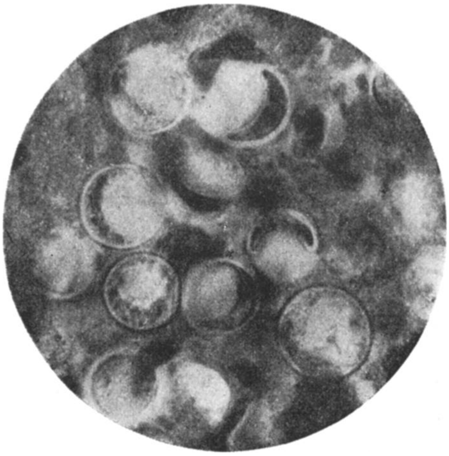

Fig. 9. Section from the nodule shown in Fig. 8. Photomicrograph, oil-immersion magnification, showing a number of double-contoured blastomyces.

upon postmortem examination had been found in the lungs. The latter when seen presented the picture of a miliary tuberculosis, the pulmonary parenchyma was riddled with grayish white opaque nodules from the size of a millet seed to a small pea. It was therefore believed that this was a case of canine miliary pulmonary tuberculosis. This condition, while not at all common, is however known to occur, and the specimen therefore was not immediately examined microscopically, but pieces of the pulmonary tissues were placed in alcohol or formalin for subsequent microscopic study. The latter was made only after the lapse of several months, when it was found that this was not a case of tuberculosis but one of blastomycosis. In the meantime the lungs from which the tissue had been taken had been lost and with them the name of the person who had sent in the lungs; hence nothing could be learned about the history of the case.

Microscopic examination of the sections showed the following: Under a low power the nodules noticed upon macroscopic inspection of the lungs appeared somewhat like tubercles, and the cells composing them seemed to be epithelioid and lymphoid cells. However, while the center of the nodules here and there was somewhat necrotic, there was nothing that looked like caseous material. There was one feature which distinguished the nodules, even under a low power, from tubercles; they were quite vascular. The nodules under low power also showed a considerable amount of coal dust.

Oil-immersion magnification showed in the nodules lymphoid and epithelioid cells, and also numerous polymorphonuclear leukocytes. The blood vessels were densely filled with red blood corpuscles, but the increase of leukocytes in the blood vessels of the nodules was relatively moderate. The most striking cellular element found in large numbers in the nodules was a spherical blastomyces, characterized by strongly marked double contours. The protoplasm of this micro-organism filled its capsule uniformly, and the crescentic appearance of the protoplasm as seen under the microscope and reproduced in the photomicrographs (Fig. 9) appeared to be largely due to an optical effect, and not to a real shrinkage of the protoplasm into the shape of a crescent.